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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,235	06/02/2000	Tayyaba Hasan	10284016001	6500

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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	17

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/586,235	HASAN ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-16 and 18-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-16 and 18-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed February 28, 2003 in Paper No. 14 is acknowledged and has been entered. Claims 6 and 17 have been canceled. Claims 1, 7, 11, 12, and 14 have been amended. Claims 18-28 have been added.

2. The declaration under 37 CFR § 1.132 by Tayyaba Hasan, Bernhard Ortel, and Edward Maytin filed February 28, 2003 in Paper No. 15 is acknowledged and has been entered.

3. Claims 1-5, 7-16, and 18-28 are pending in the application and are currently under prosecution.

Response to Declaration under 37 CFR § 1.132

4. The declaration under 37 CFR § 1.132 by Tayyaba Hasan, Bernhard Ortel, and Edward Maytin filed February 28, 2003 in Paper No. 15 is insufficient to overcome the grounds of rejection of claims 1-4, 6-8, and 10-15 under 35 USC § 103(a) for the reasons set forth in the previous Office action mailed October 29, 2002 (Paper No. 13).

The declaration states, "work reported in Ortel et al., particularly work that may be common to the present application, was performed by or under the direction, supervision or control of the inventors on the present application" (declaration, page 2, section 3). However, the declaration is insufficient because the declaration fails to clearly state that N. Chen, J. Brissette, and GP Dotto did not make *an independent inventive contribution* to the invention claimed in this application.

Additionally, a typographical error is noted in section 2 of the declaration, which renders the declaration confusing. Appropriate correction is suggested.

Grounds of Objection and Rejection Withdrawn

5. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed October 29, 2002 (Paper No. 13) have been withdrawn.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 7-13, and 18-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite terms or limitations that do not appear to be properly and sufficiently supported by the originally filed specification, such that the recitation of the terms or limitations in the claims appears to introduce new matter and thereby violates the written description requirement set forth under 35 USC § 112, first paragraph.

These terms and limitations include the following:

(a) Claims 1, 18, and 26 recite, "controlling".

(b) Claims 1 and 18 recite, "whereby the cell is of the type of cell proliferation to be controlled".

(c) Claims 1, 18, and 26 recite, "a subject in need thereof".

(d) Claims 1, 18, and 26 recite, "killing the cell".

(e) Claims 12 and 25 recite, "dihydrotestosterone".

These issues might be resolved if Applicants were to point to particular disclosures in the specification that are believed to provide the necessary explicit, expressive, or intrinsic support for the terms and limitations.

8. Claims 1-5, 7-13, and 18-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a subject diagnosed with cancer, wherein said method comprises administering to said subject an agent that induces differentiation of the subject's cancer cells and further comprises administering 5-aminolevulinic acid to the subject, does not reasonably provide enablement for a method for treating a subject having unwanted cell proliferation comprising inducing differentiation in a cell and providing said cell with a photosensitizer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reasons set forth in section 12 of the preceding Office action mailed October 29, 2002 (Paper No. 13).

Applicants have traversed these grounds of rejection arguing that the clinical use of photosensitizers and differentiating agents is conventional. Applicants have contended that undue experimentation would not be required to practice the novel embodiments of the claimed invention, because Applicants submit that the skilled artisan would not try to treat androgen-independent, or –non-responsive prostate cancer with the claimed invention. Applicants have also argued that claim 1 does not require the practitioner to administer an androgen, per se, but rather only requires the administration of an agent that induces differentiation in a cell. Applicants have contended that the grounds of rejection of the claims under 35 USC § 103(a) set forth in the previous Office action support Applicants' assertion that the instant disclosure is adequately enabling. Applicants have argued that since the targeting agent of claim 9 is not used to ameliorate or inhibit tumors, any reliance upon the references teaching the limitations of monoclonal antibodies and other tumor-antigen targeted therapies is misguided. Finally, Applicants have asserted that the amendment to the claims has resolved any inadequacy of the disclosure.

Applicants' arguments have been carefully considered but not found persuasive in view of the preponderance of evidence for the following reasons:

As a preliminary note, in reply to Applicants' remarks that the clinical use of photosensitizers and differentiating agents is conventional, the Examiner agrees the specification provides an enabling disclosure of methods that are well known in the art. The embodiments of the claimed inventions, which are novel and not well known in the art, are the subject of this rejection.

As noted in the previous Office action, the factors to be considered in determining whether undue experimentation would be required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

As noted in the Office action mailed October 29, 2002 (Paper No. 13), the amount of guidance, direction, and exemplification provided in the disclosure is not reasonably commensurate with the scope of the claims and insufficient to enable the skilled artisan to practice the claimed invention with a reasonable expectation of success without the need to perform additional, undue experimentation. Furthermore, the declaration under 37 CFR § 1.132 by Dr. Ortel, which was filed August 27, 2002 in Paper No. 10 fails to provide a showing of evidence that is reasonably commensurate in scope with the claims. While the declaration under 37 CFR § 1.132 by Dr. Ortel states that the combination of differentiation therapy and photodynamic therapy is more effective than either therapy alone, the showings are limited to studies of an androgen-responsive prostate cancer cell line and a transplantable mammary sarcoma and are therefore not reasonably commensurate in scope with the claims.

For example, although the specification exemplifies a subject having an unwanted cell proliferation as a patient having a tumor, broadly interpreted, the claims encompass a method for treating a subject that is obese and who desires, for example, to reduce the proliferation of his or her adipocytes. The teachings of the specification cannot be extrapolated to the enablement of a method for treating an obese patient as

there is no evidence that would suggest a method comprising inducing the differentiation of a cell, providing the cell with a photosensitizer, and activating the photosensitizer can effectively ameliorate the subject's obesity.

In traversing these grounds of rejection, Applicants have submitted that the skilled artisan would not try to treat androgen-independent, or –non-responsive prostate cancer with the claimed invention. Furthermore, although Applicants have argued that claim 1 does not require the practitioner to administer an androgen, *per se*. In reply to Applicants' remarks, the present claims encompass a method for controlling androgen-independent prostate cancer, and the specification fails to provide guidance and direction as to which differentiating agent is best suited for use in practicing the claimed invention to treat androgen-independent prostate cancer. Nevertheless, as stated in the previous Office action, it would be obvious to use a differentiating agent that is most likely to induce the differentiation of the targeted cells, and it is not necessary that Applicants disclose that which is well known in the art.

However, as stated in the previous Office action, the claims encompass the use of a rather broad genus of photosensitizers and precursors thereof; and the specification only demonstrates the use of a single precursor of a photosensitizer, namely ALA. If the mechanism by which a differentiating agent causes increased accumulation of protoporphyrin in cells induced to differentiate relative to control cells involves the increased expression of ferrochelatase, an enzyme that participates in the conversion of ALA into protoporphyrin, it is possible that some photosensitizing agents or precursors thereof will not accumulate preferentially in differentiating cells because the uptake and/or conversion of some may not be dependent upon the enzyme. Absent a showing that is reasonably commensurate in scope with the claims, the skilled artisan would not accept the assertion that any photosensitizer will accumulate preferentially in a cancer cell upon the induction of its differentiation, regardless of which differentiating agent has been used.

On the other hand, the teachings of Momma, et al indicate that not every differentiating agent can be used in practicing the claimed invention. Consequently, the preponderance of evidence does not support Applicants' assertion that any combination

of photosensitizing agent and differentiating agent will reproduce the observed effect of a differentiating agent and ALA.

With regard to Applicants' argument that the grounds of rejection of the claims under 35 USC § 103(a) set forth in the previous Office action support Applicants' assertion that the instant disclosure is adequately enabling, the fact that the reference discuss a variety of differentiation agents that can be used to treat breast cancer and leukemia does not suggest the claimed invention is adequately enabled by the present disclosure to meet the requirements set forth under 35 USC § 112, first paragraph. As Applicants have argued, the clinical use of differentiating agents is conventional, but the novel embodiments of the presently claimed invention are not conventional. Moreover, the grounds of rejection under 35 USC § 103(a) indicate that the prior art would have rendered obvious, and therefore enabled the embodiment of the invention, wherein the differentiating agent administered to the subject is capable of inducing the differentiation of the type of cells to be treated. For example, in view of the teachings of Mueller, et al and Santini, et al, it would have been obvious to select troglitazone or ATRA to induce the terminal differentiation of breast cancer cells or promyelocytic leukemia cells, respectively. Accordingly, the instant rejection states the specification is enabling for a method for treating a subject having cancer comprising administering to said subject an agent that induces differentiation of cancer cells and further comprises administering 5-aminolevulinic acid to the subject, but the specification fails to provide an enabling disclosure that is reasonably commensurate in scope with the claims.

In response to Applicants' suggestion that any reliance upon the references teaching the limitations of monoclonal antibodies and other tumor-antigen targeted therapies is misguided, at page 14, the disclosure contemplates the use of a monoclonal antibody as a targeting moiety. Vitetta, et al teach the limitations associated with the use of monoclonal antibody-mediated therapy; contrary to Applicants' assertion, these limitation are duly expected to affect the efficacy of the claimed invention, even if the antibody, itself, is not cytotoxic or cytostatic in nature. Furthermore, Bodey, et al teach that cancer cells expressing the antigens that are targeted by monoclonal antibodies are often "deselected"; consequently, the teachings

of Bodey, et al are germane to the present enablement inquiry. The use of the claimed invention has not been exemplified, and there appears to be no factual evidence of record that supports the assertion that the disclosure provides an enabling disclosure of the claimed invention, in view of the state and nature of the art as taught by Vitetta, et al and Bodey, et al.

Claim 11 is presently drawn to a method comprising administering to subject an antidiabetic compound or the ligand of a transcription factor, which induce differentiation. Contrary to Applicants' suggestion in their remarks, the use of these embodiments of the claimed invention is not exemplified in the disclosure. As noted in the previous Office action, while some antidiabetic compounds, such as troglitazone are peroxisome proliferators and bind the transcription factor PPAR-γ, for example, many other antidiabetic compounds are not. One skilled in the art would not accept the assertion that administering any antidiabetic compound to a subject can increase the effectiveness of photodynamic therapy, or be used in conjunction with a photosensitizer or precursor thereof to successfully treat unwanted cell proliferation. For example, there is no evidence of record that would suggest that insulin, or a sulfonylurea compound, such as glimepiride, or any other antidiabetic that acts by a mechanism different from that of troglitazone would increase the sensitivity of unwanted cells to photodynamic therapy. Moreover, there is no evidence of record that would suggest that administering any other ligand of any other transcription factor could be used in conjunction with a photosensitizer to rid the subject of unwanted cells. The activation of a transcription factor that does not regulate differentiation, for example, would not be expected to increase the accumulation of the photosensitizer in a cell; and one skilled in the art would not accept the assertion that any antidiabetic compound or any ligand of any transcription factor can be used in practicing the claimed invention to successfully eradicate or ameliorate a condition characterized by unwanted cell proliferation. The recitation of a limitation requiring the practitioner to select an antidiabetic compound or the ligand of a transcription factor, which induce differentiation, amount to no more than an invitation to the artisan to discover a suitable antidiabetic compound or the ligand of a transcription factor. The specification provides no guidance or direction, however, that

might facilitate the discovery of such a differentiating agent. The antidiabetic compounds, for example, are a largely variant class of molecules having markedly different structures and bioactivities. As there is no disclosure of a structural feature common to at least a substantial number of members of the genus of antidiabetic compounds that can be used in practicing the claimed invention, screening antidiabetic compounds to discover new differentiating agents that can be used to practice the claimed invention falls into the realm of undue experimentation.

9. Claims 11 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in section 14 of the preceding Office action mailed October 29, 2002 (Paper No. 13).

Applicants have traversed these grounds of rejection arguing that because the claims presently recite a limitation requiring the antidiabetic compound or ligand to induce differentiation of the targeted cells, the written description requirement set forth under 35 USC § 112, first paragraph has been met.

Applicants' arguments have been carefully considered but not found persuasive, because the inclusion of a limitation requiring the compounds to induce differentiation of the targeted cells is not descriptive of the genus of compounds and ligands; rather it is merely a recitation of what the members of the genus must be capable of doing, but without structurally delineating the genus so that the skilled artisan might envision, or immediately recognize at least a substantial number of the members of the genus of compounds and ligands. As noted in the previous Office action, the antidiabetic compounds are a highly variant class of molecules having markedly different structures and bioactivities; the member of the genus of ligands is even more structurally and functionally variant. The specification discloses but a single member of the genus of antidiabetic compounds and ligands, and fails to teach what structural features of the compound are common to at least a substantial number of the members of the genus

so that the skilled artisan would reasonably conclude that Applicants had possession of the claimed invention at the time the application was filed.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-5, 7-11, and 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons set forth in section 16 of the preceding Office action mailed October 29, 2002 (Paper No. 13).

Applicants have traversed this ground of rejection arguing that the specification defines "unwanted", giving examples of disorders characterized by unwanted cell proliferation.

Applicants' arguments have been carefully considered but not found persuasive. As stated in the preceding Office action, the term unwanted is a subjective term; what may be considered "unwanted" by one person, may not be considered so by another. Although claim 2 requires the subject of claim 1 to be a patient having a malignant or benign disorder characterized by unwanted cell proliferation, malignant and benign disorders include any and all disorders. Because "unwanted is a subjective term, which is not defined, and because the metes and bounds of an "unwanted cell proliferation" are not clearly delineated by the claims and only non-limited examples of "unwanted cell proliferation" are provided in the disclosure, the metes and bounds of the invention are not sufficiently delineated by the claims to meet the requirements set forth under 35 USC § 112, second paragraph.

12. Claims 1-6, 8-12, and 18-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6, 8-12, and 18-25 are indefinite because claims 1 and 18 recite, "whereby the cell is of the type of the cell proliferation to be controlled". The recitation

of the phrase renders the claims indefinite because the phrase is seemingly nonsensical, or confusing anyway, as a cell is not a type of cell proliferation. Accordingly, the metes and bounds of the invention would not be clearly delineated by the claims.

As an additional note, if the term a "cell proliferation" is used as a noun to mean, for example, a tumor, this usage does not appear to be supported by the originally filed specification, because "cell proliferation" appears to only have been used in the specification to denote the process of cell proliferation.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1-3, 6, 7, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Koulu (*Photodermatology* **1**: 42-43, 1984) for the reasons set forth in section 19 of the preceding Office action mailed October 29, 2002 (Paper No. 13).

Applicants have traversed this ground of rejection arguing the prior art does not teach every element of the claimed invention, since the method of Koulu does not treat unwanted cell proliferation.

Applicants' arguments have been carefully considered but not found persuasive for the following reasons:

Koulu teaches a method comprising administering a differentiating agent, namely a retinoid to a patient having psoriasis, administering a photosensitizer, namely psoralen to the patient, and irradiating the patient. Furthermore, Koulu teaches the combination has been demonstrated to be effective in treating psoriasis, a disorder characterized by unwanted cell proliferation.

As evidence by the teachings of Koulu combining a differentiating agent and a photosensitizing agent to treat benign psoriasis is not novel.

The method of the prior art comprises the same method steps as claimed in the instant invention, and because the differentiating agent will induce differentiation and the radiation will activate the photosensitizer, the claimed method is anticipated because the method will inherently lead to controlling unwanted cell proliferation. See *Ex parte Novitski*, 26 USPQ 1389 (BPAI 1993).

Applicants may obviate this rejection by amending the claims to recite the provision that the cell induced to differentiate is not a psoriatic cell. Support for such a limitation can be found in the specification at page 4, lines 17 and 18.

15. Claims 1, 2, 13-15, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 5,784,162-A for essentially the reasons set forth in section 20 of the preceding Office action mailed October 29, 2002 (Paper No. 13).

US Patent No. 5,784,162-A ('162) teaches that which is set forth in section 20 of the preceding Office action. Additionally, '162 teaches that the treated cells are melanoma cells.

Applicants have traversed this ground of rejection arguing the prior art does not teach every element of the claimed invention, since the Examiner has not provided evidence of the fact that DMSO is a differentiating agent. Additionally, Applicants have argued that the prior art does not teach that the combination of DMSO and photosensitizing agent will have the effect that practicing the claimed invention must have.

Applicants' arguments have been carefully considered but not found persuasive for the following reasons:

DMSO is a differentiating agent. A search of MEDLINE will result in several publications that teach that DMSO is a differentiating agent. For example, using "DMSO-induced differentiation" as a search query, the earliest publication that could be found is the article entitled, "Control of Globin Synthesis during DMSO-induced Differentiation of Mouse Erythroleukemic Cells in Culture", which was published by Gaedicke, et al (*Hamatol Bluttransfus* 1974; **14**: 278-87).

Should Applicants maintain that DMSO is not a differentiating agent, it is noted that the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the product of the instant claims. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the product of the instant claims is different than that taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

Furthermore, in response to Applicants' argument that the prior art does not teach the outcome of treating a subject with the combination, as observed by Applicants, the method of the prior art comprises the same method steps as claimed in the instant invention, namely administering a combination of a differentiating agent and a photosensitizing agent and irradiating the subject. Because the differentiating agent will induce differentiation and the radiation will activate the photosensitizer, the claimed method is anticipated because the method will inherently lead to controlling unwanted cell proliferation. See *Ex parte Novitski*, 26 USPQ 1389 (BPAI 1993).

Furthermore, in *Atlas Powder Co. v. IRECO*, 51 USPQ2d 1943 1947 (Fed Cir, 1999), the Court has decided:

> Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. [...] However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-4, 6-8, and 10-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortel, et al (*British Journal of Cancer* **77**: 1744-1751, June 1998) and Momma, et al (*International Journal of Cancer* **72**: 1062-1069, 1997) in view of Mueller, et al (*Molecular Cell* **1**: 465-470, 1998), and Santini, et al (*British Journal of Haematology* **102**: 1124-1138, 1998) for the reasons set forth in section 22 of the preceding Office action mailed October 29, 2002 (Paper No. 13).

Applicants have traversed this ground of rejection asserting that the declaration under 37 CFR § 1.132 by Tayyaba Hasan, Bernhard Ortel, and Edward Maytin filed February 28, 2003 in Paper No. 15 is insufficient to overcome the grounds of rejection of claims 1-4, 6-8, and 10-15 under 35 USC § 103(a) for the reasons set forth in the previous Office action mailed October 29, 2002 (Paper No. 13).

Applicants' arguments and the merit of the declaration have been carefully considered but not found persuasive or sufficient to overcome the grounds of rejection. The declaration states, "work reported in Ortel et al., particularly work that may be common to the present application, was performed by or under the direction, supervision or control of the inventors on the present application" (declaration, page 2, section 3). However, the declaration is insufficient because the declaration fails to clearly state that N. Chen, J. Brissette, and GP Dotto did not make *an independent inventive contribution* to the invention claimed in this application.

This ground of rejection could be overcome if Applicants were to submit a declaration that clearly states that N. Chen, J. Brissette, and GP Dotto did not make *an independent inventive contribution* to the invention claimed in this application.

Conclusion

18. No claims are allowed.

19. Applicants' request for an interview is noted, and Applicants' representative is invited to contact the Examiner to schedule an interview at Applicants' convenience or behest.

20. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
May 19, 2003

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600